

Applicant: Cy A. Stein
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REMARKS

Claims 9, 26-30 and 32-65 are currently pending and under examination in the subject application. By this Amendment, applicant has hereinabove canceled claims 32-35, and 53 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future continuation or other application, and have amended claims 9, 26, 36-43, 51, 52, 54 and 64, and have added new claims 66-72. Support for the amendments to claim 9 can be found in the specification as originally filed at, *inter alia*, page 3, lines 2-5; page 5, line 3; and page 20, lines 7-8. Support for the amendments to claim 26 can be found in the specification as originally filed at, *inter alia*, page 3, lines 2-5; page 5, line 3; page 18, lines 1-6; and page 20, lines 7-8. Support for the amendments to claim 36 can be found in the specification at, *inter alia*, page 15, lines 5-8. Support for the amendments to claim 37 can be found in the specification at, *inter alia*, page 1, line 39 to page 2, line 2; and page 15, lines 5-8. Support for the amendments to claim 38 can be found in the specification at, *inter alia*, page 1, line 39 to page 2, line 2; and page 15, lines 5-8. Support for the amendments to claim 39 can be found in the specification at, *inter alia*, page 13, lines 27-30; and page 15, lines 5-8. Support for the amendments to claim 40 can be found in the specification at, *inter alia*, page 13, lines 32-35; and page 15, lines 5-8. Support for the amendments to claim 41 can be found in the specification at, *inter alia*, page 13, line 37 to page 14, line 3; and page 15, lines 5-8. Support for the amendments to claim 42 can be found in the specification at, *inter alia*, page 14, lines 5-8; and page 15, lines 5-8. Support for the amendments to claim 43 can be found in the specification at, *inter alia*, page 14, lines 10-13; and page 15, lines 5-8. Support for the amendments to claim 51 can be found in the specification at, *inter alia*, page 14, lines

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20-24 and Figure 1. Support for the amendments to claim 52 can be found in the specification at, *inter alia*, page 13, lines 22-25 and Figure 1. Support for the amendments to claim 54 can be found in the specification at, *inter alia*, page 8, lines 36-37. Support for the amendments to claim 64 can be found in the specification as originally filed at, *inter alia*, page 3, lines 2-5; page 5, line 3; page 18, lines 1-6; and page 20, lines 7-8. Support for new claim 66 can be found in the specification as originally filed at, *inter alia*, page 19, lines 22-25. Support for new claim 67 can be found in the specification as originally filed at, *inter alia*, page 16, lines 1-6. Support for new claim 68 can be found in the specification as originally filed at, *inter alia*, page 15, lines 19-24. Support for new claim 69 can be found in the specification as originally filed at, *inter alia*, page 15, lines 26-29. Support for new claim 70 can be found in the specification as originally filed at, *inter alia*, page 16, lines 1-4. Support for new claim 71 can be found in the specification as originally filed at, *inter alia*, page 16, lines 6-8. Support for new claim 72 can be found in the specification as originally filed at, *inter alia*, page 16, lines 10-14. Applicant maintains that the Amendments to the claims raise no issue of new matter, and respectfully request entry of this Amendment. Accordingly, after entry of this Amendment, claims 9, 26-30, 36-52, and 54 to 72 will be pending and under examination.

Claims Rejected Under 35 U.S.C. §103(a)

The Examiner stated that claims 37-45, 55, 58, and 63-65 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pollman et al. and Gibbons et al. (U.S. Patent No. 5,776,905) in view of Agrawal, and Summerton. The Examiner stated that claim 63 and 64 are drawn to a composition comprising an antisense oligonucleotide comprising consecutive nucleotides, the nucleotide sequence of which is set forth in SEQ ID NO:2. The

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Examiner further stated that claim 65 is drawn to a method of promoting the regression of vascular lesions comprising introducing antisense oligonucleotides shown to be effective in reducing bcl-xL expression into a vascular cell.

The Examiner stated further that Pollman et al. teach inhibition of neo-intimal cell bcl-x expression comprising transfecting a composition comprising Lipofectamine and an antisense oligonucleotide directed against bcl-x into atheromatous (i.e. vascular) lesions in the rabbit carotid artery, and that specific down regulation of the bcl-xL splice isoform resulted in regression of atheromatous lesions. The Examiner stated that additionally, Pollman et al. discloses three phosphorothioate modified antisense oligonucleotides, wherein antisense sequence #3, page 226, comprises the consecutive nucleotide sequence of SEQ ID NO: 2 of the instant application.

In response, applicant respectfully traverses the Examiner's rejection. Initially, applicants note that claims 63-65 recite an oligonucleotide consisting of SEQ ID NO:2, not "comprising SEQ ID NO:2" as the Examiner has stated. Thus, Pollman et al. does not teach the claimed invention, and, even if combined with the remaining cited references as stated by the Examiner, does not teach SEQ ID NO:2. Accordingly, applicant respectfully request that the examiner reconsider and withdraw this ground of rejection. In addition, in order to expedite prosecution, but without conceding the correctness of the Examiner's argument, applicants have hereinabove amended claims 37-43. Applicant notes that claims 37 and 38 recite an oligonucleotide consisting of SEQ ID NO:2. Thus, Pollman et al. does not teach the claimed invention as it recites a different sequence, and, even if combined with the remaining cited references, does not teach SEQ ID NO:2. With respect to claims 39-43, none of the cited references, even if combined as stated by the Examiner, teach or

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suggest SEQ ID NOs: 1 and 3-13. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §112 (Written Description)

The Examiner stated that claims 39-50, and 53-61 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner stated that the instant claims are drawn to antisense oligonucleotides or analogs thereof comprising a sequence having 90%, 85%, 80%, 75%, or 70% or greater identity to sequences A, B, C, D, E, F, G, H, I, J, K, L, or M of Figure 1 of the instant application. The Examiner further stated that the specification as filed does not describe the sequence of any antisense oligonucleotide having a sequence that is 90%, 85%, 80%, 75%, or 70% identity to SEQ ID NO: 1-13 which would function to modulate (increase or decrease) expression of bcl-xl. The Examiner also stated that providing a method for isolating and testing the claimed compounds for the recited functionality is not sufficient for providing an adequate description of a compound, especially a biomolecule such as a nucleic acid compound where applicants do not provide a correlation between the nucleotide sequence of a compound and its functional activity, i.e. increase or decrease expression of bcl-xl.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, but without conceding the correctness of the Examiner's argument, applicants have hereinabove amended claims 39-43 to recite the characteristic that the compounds are complementary to a bcl-xl mRNA feature, thus defining the sequence of the antisense molecules. Accordingly, applicant maintains that the invention is clearly described, and respectfully requests that the Examiner

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reconsider and withdraw this ground of rejection.

Double Patenting

The Examiner stated that claims 9, 26-30, 36, 63, and 65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-54, and 61-62 of copending Application No. 10/160,344. The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are drawn to compositions of matter comprising an antisense oligonucleotide comprising the nucleotide sequence of one of SEQ ID NOS: 1 and 3-13, wherein one or more of the sugar groups of the oligonucleotide contain an -Ome group at its 2' position. The Examiner further stated that claims are also directed to compositions comprising antisense oligonucleotides comprising the nucleotide sequence of SEQ ID NO:2 wherein one or more of the sugar groups of the oligonucleotide contain an -Ome group at its 2' position.

Applicant notes that the claims of copending U.S. Application Serial No. 10/160,344 were amended via an Amendment filed on June 30, 2004 with the United States Patent and Trademark Office. The claims of 10/160,344 as amended do not recite oligonucleotides wherein one or more sugar of the oligonucleotide contain an -OME group at its 2' position, as recited in claims 9, 26, 36, and 63 of the subject application. In addition, the sugar modification of an -OME group at its 2' position is unobvious over the claims of 10/160,344. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.